Correspondence

Methylphenidate for Hiccups

To the Editor:—Recently, a year-old paper [1] in which methylphenidate was found ineffective in the treatment of hiccups came to my attention. We [2] had found 20 mg methylphenidate to be highly effective in suppressing hiccups in a variety of patients, compared with a placebo ($P < 0.001$). Gregory and Way [1] did not obtain significant results when using 10 mg of the drug in patients with hiccups during operation, even when they repeated the dose, as was necessary in many cases.

The above-named authors discredited our results but failed to discuss the importance of the following, which may reconcile the differences. 1) They used only half of the dose we used. It is a pharmacological principle that the plasma concentration of a given intravenous dose of drug is unlikely to be achieved by two half-doses given separately. This is particularly true with short-acting drugs. The possibility of tachyphylaxis should also be considered. 2) Their experience was limited to the use of the drug during operation, when hiccups frequently subside without treatment. In the majority of our cases hiccups had been caused by a variety of pathologic conditions and had lasted for hours or days prior to the administration of methylphenidate or placebo. Finally, these authors stated that we gave 10–20 mg of methylphenidate. We remarked very clearly, however, that satisfactory results were obtained after administration of 20 mg to all our patients except one, who received 30 mg. In our experience 10 mg is inadequate for suppression of hiccups.

Methylphenidate is a useful drug in the treatment of a variety of patients with hiccups of short or long duration, whether or not related to operation and anesthesia, provided it is given in adequate dose. Methylphenidate was also effective in 100 per cent of patients who have muscular spasticity during recovery from halothane anesthesia, within two minutes of administration.[3] Likewise, it has been dramatically effective in other states involving involuntary contraction of striated muscles, such as shivering.[4, 5]

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To the Editor:—In response to Dr. Macris' letter regarding methylphenidate, we would like to re-emphasize the major point of our paper, *i.e.*, that 10–20 mg of methylphenidate was no more effective in the treatment of hiccups than a placebo. It had been reported by Vasiloff *et al.* that 10 mg of methylphenidate was effective in stopping singultus and therefore, was being touted as such by drug company representatives.

Dr. Macris suggests that his results were different from ours for two reasons. First, because with 20 mg of methylphenidate, the plasma level would be greater than with 10 mg. This, of course, is true. However, there were patients in his group in whom hiccups ceased during injection of the drug, before the entire dose was given and apparently in less than a circulation time. Those patients obviously had lower plasma levels than achieved with 20 mg of drug, yet they still got an effect.

Similarly, Vasiloff and his co-workers achieved an effect in some patients before the full 10 mg had been given. While giving two 10-mg doses three minutes apart will not give the same plasma level as one 20-mg dose, the former will certainly give a higher plasma level than that following a single 10-mg dose of drug, similar to the level at which Macris *et al.* saw an effect during injection.

Second, Dr. Macris' point that most of his patients were awake, while ours were anesthetized, is correct. Those of Vasiloff *et al.* were, however, anesthetized. We agree that there may be a difference between effects in conscious and anesthetized patients.

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MAC and Dose–Response Curves

To the Editor:—The editorial by Waud and Waud in the July 1970 issue of ANESTHESIOLOGY was most necessary. Potency ratios, if obtainable, would be of great practical value to anesthesiologists in helping them choose the more desirable anesthetic agents. Side-effects and toxicity must be related to potency before a meaningful selection process can occur.

I, too, believe that Eger's concept of MAC has been an imaginative and useful contribution. However, minimum alveolar concentration is a poor term for the measurement. There is no indication that the concentration at which the patient does not move is the minimum alveolar concentration for that patient, because only one concentration is administered to each patient. Actually, Eger and colleagues and others have been determining (albeit roughly) the median effective alveolar concentration.

The median effective dose (ED_{50}), when determined appropriately, permits comparison of the potencies of drugs in different groups of subjects, converting the dose response to a straight line by a log dose—probit transformation.[1] In addition, the method provides a test for goodness of fit, checks for parallelism of two dose responses and estimates the confidence limits of ED_{50} before calculating potency ratios.

This concept has utility in establishing a point to compare side effects and toxicity. For example, the dose at which 50 per cent of patients are effectively anesthetized might cause 30 per cent side effects with one drug and 5 per cent with another drug.. This kind of information would be of considerable practical importance in helping anesthesiologists toward a more rational selection of anesthetics. My colleagues and I have used this concept to show that the median effective alveolar concentrations of halothane differ for adults and children.[2]

Undoubtedly, a dose–response curve featuring variable depths of anesthesia plotted against alveolar concentrations would be extremely useful. Major barriers now prevent realization of this ideal in human and animal experimentation. The changes in alveolar concentration would have to be established for at least 15–20 minutes before initiation of a stimulus in order to ensure that alveolar–brain equilibrium had occurred. No quantitative method of measuring depth of anesthesia that allows a variable plot exists.

Under the circumstances, the only acceptable method of comparing anesthetic potency with side-effects and toxicity is by use of the ED_{50} concept. This concept has had acceptance by pharmacologists for several decades and can provide useful information for anesthesiologists.

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